UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

August 22, 2005

MEMORANDUM

SUBJECT: Exemptions from the Requirement of a Tolerance for
C9 Rich Aromatic Hydrocarbons, PC Code 886810, PP# 4E6935, DP Barcode 316616
C10-11 Rich Aromatic Hydrocarbons, PC Code 806602, PP# 4E6934, DP Barcode 316615
C11-12 Rich Aromatic Hydrocarbons, PC Code 806602 & 806501, PP# 4E6937; DP Barcode 316617
MRIDs 46369812, 46369813, 46398901, 46398902, 46398903, 46398904, 46398905, 46398906, 46398907, 46398908, 46398909, 46398910, 46398911

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This provides a science assessment for C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons based on data submitted for the corresponding Exxon Mobil trade name products, Aromatic 100 Fluid, Aromatic 150 Fluid, and Aromatic 200 Fluid respectively. The attached assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, and environmental fate of these three pesticide inert ingredients. The purpose of this document is to evaluate the proposed exemptions from the requirement of a tolerance for residues of the three inert ingredients as required under the Food Quality Protection Act (FQPA) section 408. This is a conservative risk assessment in which high-end assumptions were used for most key parameters. HED is confident that this analysis does not underestimate the risk associated with exposure to C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons.

1.0 EXECUTIVE SUMMARY

This assessment evaluates potential risks from use of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons. These three inert ingredients have been considered to be included under the existing tolerance exemptions for petroleum oils and xylene. ExxonMobil submitted dietary and residential exposure/risk assessments for the trade name products Aromatic 100 Fluids, Aromatic 150 Fluids, and Aromatic 200 Fluids; the generic names for these products are C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons respectively. ExxonMobil has petitioned to have these chemicals exempted from the requirement of a tolerance. HED has evaluated ExxonMobil's submissions and has incorporated information from those assessments into its risk assessment. Toxicological data submitted by ExxonMobil provide the primary basis for HED's hazard identification evaluation.

Aromatic 100, 150, and 200 Fluids are ExxonMobil's trade names for C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons which are a multi-constituent group of related hydrocarbon compounds with closely controlled and defined physicochemical parameters. The C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons consist of a mixture of aromatic hydrocarbons. C9 Rich Aromatic Hydrocarbons consist primarily of alkylated benzenes that have a predominant carbon number in the range of C_9 to C_{10}. C10-11 Rich Aromatic Hydrocarbons consist primarily of alkylated benzenes with some alkylated naphthalenes that have a predominant carbon number in the range of C_{10} to C_{11}. C11-12 Rich Aromatic Hydrocarbons consist primarily alkylated benzenes with some alkylated naphthalenes that have a predominant carbon number in the range of C_{10} to C_{12}. C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons are created as part of the crude oil refining process and are widely used as pesticide inert ingredients.

Sufficient toxicity data and information on Aromatic 100, 150, and 200 Fluids are available from the petitioner. As noted, Aromatic 100 Fluid consists primarily of linear alkyl benzenes; Aromatic 150 and 200 Fluids consist primarily of primarily alkylated benzenes with some alkylated naphthalenes. Both EPA and OECD have expressly identified linear alkyl benzenes as an example of appropriate Structural Activity Relationship (SAR) categories of chemicals. Based on common functional substructure, common metabolic pathways/kinetics of metabolism, and comparable molecular properties, the aromatic fluids can be considered valid analogues of each other for purposes of predicting toxicity. C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are therefore considered toxicologically equivalent and are assessed together in this document. HED also assessed potential risks from naphthalene, which comprises up to 10% of Aromatic 150 and 200

Fluids. The toxicological data base is adequate to assess risks from exposure to naphthalene as a component of these Aromatic Fluids.

Based on data submitted by the petitioner on the trade name products, Aromatic 100, 150, and 200 Fluids exhibit low acute toxicity by oral, inhalation and dermal routes (toxicity Category III or IV by all exposure routes). They are minimally irritating to eyes and skin and negative for dermal sensitization effects. Subchronic oral and inhalation toxicity studies indicate these Aromatic Fluids to be relatively non-toxic except at relatively high doses. Reversible effects to the liver, thyroid, stomach, spleen, and urinary bladder were reported at mid- and high doses in a subchronic oral toxicity study in rats. A developmental inhalation study in mice indicates severe maternal and developmental toxicity at the high dose (1500 ppm) and reduction in fetal weight gain at the next lowest dose (500 ppm) but no other evidence of developmental effects nor any adverse effects in maternal animals. An oral developmental study in rats indicates maternal effects (decreased body weight gain and food consumption) at the mid-dose (150 mg/kg/day) but no developmental effects at the highest dose tested (450 mg/kg/day). An inhalation reproduction study in rats indicates reduced body weight gain in parents and off-spring at mid and high doses (500 and 1500 ppm). Based on neurotoxicity studies, Aromatic 100, 150, and 200 Fluids are not expected to cause any nervous system damage. Due to their complex, multi-constituent nature, there are no substance-specific absorption, metabolism, distribution and excretion studies done specifically on Aromatic 100, 150, and 200 Fluids. However, sufficient data are available on aromatics to show that they are typically well absorbed, widely distributed between tissues, extensively metabolized and rapidly excreted. Aromatic 100, 150, and 200 Fluids are of low toxicological concern for developmental and reproductive effects, based on the available toxicity data. Based on this finding, it is recommended that the Food Quality Protection Act (FQPA) tenfold safety factor be reduced to 1x for this risk assessment.

The assessments of C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons have been grouped together in this document because they are toxicologically equivalent, and share similar use patterns and potential routes of exposure. HED conducted screening level dietary and residential exposure and risk assessments for the Rich Aromatic Hydrocarbons. HED did not aggregate estimated exposure/risk for these chemicals, however, because it is unlikely that products containing C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons will be used concurrently. HED also assessed potential risks from naphthalene, which comprises up to 10% of C10-11, and C11-12 Rich Aromatic Hydrocarbons. Based on HED’s screening level quantitative assessment, C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons do not pose dietary risks of concern. A screening level quantitative assessment of inhalation and dermal exposures to residential applicators indicates no risks of concern. A qualitative exposure assessment of incidental oral exposures indicates that these compounds also do not pose risks of concern for this route of exposure. In addition, ecological risk concerns are not likely to occur from the use of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons as pesticide inert ingredients based on available toxicity data on aquatic and terrestrial organisms. Therefore, it is recommended that C9 Rich Aromatic Hydrocarbons, C10-

11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons in/on raw agricultural commodities can be considered safe under section 408(q) of the FFDCA.

2.0 USE INFORMATION

C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons have many uses as a pesticide inert ingredients. Most commonly, these compounds are used as solvents for a wide variety of fungicides, herbicides and pesticides. The pesticide is usually dissolved in C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons and other solvents, and later is applied as an emulsion after dilution with water. Other common solvent uses include use in ultra low volume pesticides where the pesticide is dissolved in C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons or a solvent mixture and applied at low volumes with no addition of water. The exemptions from the requirement of a tolerance for C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons Fluids are provided in Table 1 below.

Table 1. Chemicals Included in this Risk Assessment

Chemical Name (Trade Name)	CAS Reg No.	40 CFR §	Use (Pesticidal)	List Classification
C9 Rich Aromatic Hydrocarbons (Aromatic 100 Fluid)	64742-95-6	180.905[1] 180.910[2] 180.920[3] 180.930[4]	solvent/co-solvent	2
C10-11 Rich Aromatic Hydrocarbons (Aromatic 150 Fluid)	64742-94-5	180.905[1] 180.910[2]	solvent/co-solvent	2
C11-12 Rich Aromatic Hydrocarbons (Aromatic 200 Fluid)	64742-94-5 68477-31-6	180.920[3] 180.930[4]	solvent/co-solvent	2

1. Pesticide Chemicals: Residues listed in 40 CFR §180.905 [formerly 40 CFR§ 180.1001(b)] are exempted from the requirement of a tolerance when applied to growing crops, in accordance with good agricultural practice.
2. Inert Ingredients: Residues listed in 40 CFR §180.910 [formerly 40 CFR§ 180.100(c)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert or occasionally active ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
3. Inert Ingredients: Residues listed in 40 CFR §180.920 [formerly 40 CFR§ 180.100(d)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert or occasionally active ingredients in pesticide formulations applied to growing crops only.
4. Residues listed in 40 CFR §180.930 [formerly 40 CFR§ 180.100(e)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert or occasionally active ingredients in pesticide formulations applied to animals.

3.0 PHYSICAL AND CHEMICAL PROPERTIES

Table 2. Physical and Chemical Properties of Aromatic 100, 150, and 200 Fluid and Naphthalene				
	Aromatic 100 Fluid	**Aromatic 150 Fluid**	**Aromatic 200 Fluid**	**Naphthalene**
PC Code	886810	806602	806602 & 806501	055801 & 855801
CAS #	64742-95-6	64742-94-5	64742-94-5 68477-31-6	91-20-3
Chemical name	C9 Rich Aromatic Hydrocarbons	C10-11 Rich Aromatic Hydrocarbons	C11-12 Rich Aromatic Hydrocarbons	naphthalene
Molecular formula	alkylated benzenes C_9-C_{10}	alkylated benzenes C_{10}-C_{11}	alkylated benzenes C_{10}-C_{12}	$C_{10}H_8$
Molecular weight	NA	NA	NA	128.18
Physical state	Liquid	Liquid	Liquid	Liquid
Vapor Pressure (20 C)	2.09 mm Hg	0.62 mm Hg	0.043 mm Hg	0.085 mm Hg
Density	0.873 g/cm^3 15.6 C	0.899 g/cm^3 15 C	0.995 g/cm^3 15 C	
Boiling Point	161-171 C at 1013 hPa	184-205 C at 1013 hPa	232-275 C at 1013 hPa	217.9
Freezing Point	7 F	-18 C	-19 C	NA
Flash Point	46 C closed cup	63 C closed cup	95 C closed cup	NA
Water Solubility	11-69 mg/L	4.8-55 mg/L	4.8-55 mg/L	31 mg/L
Henry's Law constant	6E-03 to 33E-03 atm-m^3/mole	4E-04 to 4.6E-04 atm-m^3/mole	4E-04 to 4.6E-04 atm-m^3/mole	4.4E-04 atm-m^3/mole
Log P (octanol-water)	>3.0	>3.0	>3.0	3.3

Table 3. Fugacity Modeling (Mackay Level 1)			
	Aromatic 100 Fluid	**Aromatic 150 Fluid**	**Aromatic 200 Fluid**
Air	98.6-99.8%	78.1-96.1%	78.1-96.1%
Soil	0.1-0.5%	1.8-6.9%	1.8-6.9%
Water	0.1-0.5%	0.5-9.8%	0.5-9.8%

4.0 HAZARD ASSESSMENT

4.1. Hazard Profile

This hazard assessment was developed using toxicity data provided by the petitioner. The toxicity data base for the trade name products Aromatic 100, 150, and 200 Fluids is adequate for the selection of doses and endpoints for use in risk assessment of C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons. HED evaluated the available studies and established acute and chronic RfDs, as well as doses and endpoints for inhalation and dermal exposure scenarios. Endpoints were not selected for residential incidental oral exposure routes based on use and physical chemical property data which indicates that these scenarios are not likely to be of concern. The Acute RfD is an estimate of a single day oral exposure level for the human population that is likely to be without an appreciable risk of deleterious effects. The chronic RfD is an estimate of a daily oral exposure level that is likely to be without an appreciable risk of deleterious effects during a lifetime. Acute and chronic RfDs are calculated by dividing the No Observable Adverse Effect Level (NOAEL) by the Uncertainty Factors (UF). UFs are used to account for differences between humans (intraspecies variability) and for differences between the test animals and humans (interspecies extrapolation). For the residential inhalation exposures assessed, UFs are used to determine adequate margins of exposure (MOEs). The MOE is the ratio of the route appropriate NOAEL to the estimated exposure. HED also evaluated available studies to determine if there was a special sensitivity for infants and children. The toxicological data for Aromatic 100, 150, and 200 Fluids are summarized in Tables 4 and 5.

The toxicity data base for naphthalene is adequate for the selection of doses and endpoints for use in risk assessment. The toxicological data for naphthalene are summarized in Sections 4.2 and 4.3 below.

Table 4. Acute Toxicity Profile for AF100, 150, and 200						
Study Species	AF100 (CAS # 64642-95-6)		AF150 (CAS # 64642-94-5)		AF200 (CAS # 64642-94-5)	
	Results	Classification	Results	Classification	Results	Classification
oral rat	LD50 = 3.4 g/kg	Category III	LD50 = 7.1 g/kg (m) LD50 = 5.6 g/kg (f)	Category IV	LD50 = 10.7 g/kg (m) LD50 = 5 g/kg (f)	Category IV
Inhalation rat	LC50 = >1192 ppm	Category IV	LC50 = >809 ppm	Category IV	LC50 = 726 ppm	Category IV
dermal rabbit	LD50 = >3.16 g/kg	Category III	LD50 = >2 g/kg	Category III	LD50 = >3.16 g/kg	Category III
skin irritant rabbit	moderate		moderate		mild	
eye irritation rabbit	minimal	no irritation	slight	no irritation	minimal	no irritation
skin sensitization human	no	not a sensitizer	no	not a sensitizer	no	not a sensitizer

Table 5. Toxicity Profile for AF100, 150, and 200			
Study Type	Publication	Doses	Results
3 day inhalation neurotoxicity male rat (C10-C11 aromatics)	Nessel et al 2000	0, 35, 110, 365 ppm	NOAEL = 110 ppm (600 mg/m^3;156 mg/kg/day) LOAEL = 365 ppm low to moderate gait abnormalties
90 day oral gavage rat (1,3,5-trimethylbenzene)	IIT Research Institute, 1995	0, 50, 200, 600 mg/kg/day	NOAEL = 600 mg/kg/day no effects at highest dose tested

Table 5. Toxicity Profile for AF100, 150, and 200			
Study Type	Publication	Doses	Results
90 day oral gavage rat (Aromatic 200 Fluid)	EMBSI 1991	0, 300, 600, 1000 mg/kg/day	NOAEL = 300 mg/kg/day LOAEL = 600 mg/kg/day reversible effects to liver, thyroid, stomach, spleen, and bladder
90 day neurotoxicity inhalation rat (C9AHM)	Douglas et al 1993	0, 101, 452, 1320 ppm	NOAEL = 1320 ppm no effects highest dose tested
1 year inhalation rat (50/50 mixture AF100 & Shellsol)	Clark et al 1989	0, 450, 900, 1800 mg/m^3	NOAEL = 1800 mg/m^3 (340 ppm) no effects highest dose tested
3-generation reproduction inhalation rat(C9AHM)	McKee et al 1990	0, 100, 500, 1500 ppm	Parental LOAEL = 100 ppm reduced weight gain F_2 (143 mg/kg/day) Offspring NOAEL = 100 ppm LOAEL = 500 ppm reduced mean pup weight F_3
Developmental inhalation mouse (C9AHM)	McKee et al 1990	0, 100, 500, 1500 ppm	Developmental NOAEL = 100 ppm LOAEL = 500 ppm reduction in fetal weight gain Maternal NOAEL = 100 ppm (207 mg/kg/day) LOAEL = 500 ppm reduced maternal weight gain
Developmental oral gavage rat (Aromatic 200 Fluid)	EMBSI[1] 1992	0, 75, 15, 450 mg/kg/day	Maternal NOAEL = 150 mg/kg/day LOAEL = 450 mg/kg/day decreased body weight gain and food consumption Developmental NOAEL = 450 mg/kg/day
Bacterial reverse mutation assay (C9AHM)	EMBSI 1991		not mutagenic
In vitro cytogenetic Assay (CHO) (C9AHM)	EMBSI 1992		negative
Rat bone marrow cytogenetics assay (C9AHM)	EMBSI 1992		negative
CHO/HGPRT Forward Mutation Suspension Assay (C9AHM)	EMBSI 1992		negative
Chronic/Cancer - No Studies available	NA	NA	Not likely to be carcinogenic in humans based on SAR [2]

[1] ExxonMobil Biomedical Sciences, Inc.
[2] EPA, Review of Mutagenicity Testing Results on C_9 Aromatic Hydrocarbon Fraction, "The negative results of these studies do not trigger additional mutagenicity or carcinogenicity testing as specified in the C_9 test rule." (April 1, 1992)

4.2 Hazard Characterization

Aromatic 100, 150, and 200 Fluids exhibit low acute toxicity by oral, inhalation and dermal routes (toxicity Category III or IV by all exposure routes). These compounds are minimally irritating to eyes and skin and negative for dermal sensitization effects.

C9 Rich Aromatic Hydrocarbons (Aromatic 100 Fluid) consists primarily of linear alkyl benzenes. Aromatic 150 and 200 Fluids (C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons) consist primarily of linear alkyl benzenes with some alkylated naphthalenes. Both EPA and OECD have expressly identified linear alkyl benzenes as an example of appropriate SAR categories of chemicals. C9 Rich Aromatic Hydrocarbons tend to contain higher concentrations of trimethylbenzenes and C10-11 Rich Aromatic Hydrocarbons contain higher concentrations of tetramethylbenzenes. However, both have common functional substructure, common metabolic pathways/kinetics of metabolism, and comparable molecular properties. Therefore, C9 Rich Aromatic Hydrocarbons can be considered an appropriate analog for predicting the toxicity of C10-11 Rich Aromatic Hydrocarbons. Both C10-11 Rich Aromatic Hydrocarbons and C11-12 Rich Aromatic Hydrocarbons contain chemical constituents largely with carbon numbers between C_{10} and C_{12}. While C10-11 Rich Aromatic Hydrocarbons tend to have more of C_{10} and C_{11} constituents and C11-12 Rich Aromatic Hydrocarbons tend to have more of the constituents in the C_{11} to C_{12} range, the two compounds also share a common functional substructure (alkyl group on an aromatic), common metabolic pathways and kinetics of metabolism, and similar molecular properties. Thus, these Aromatic Hydrocarbons can be considered valid analogues of each other for purposes of predicting toxicity. Furthermore, C_9 aromatic hydrocarbon materials (C_9AHM) can be considered a valid analog for the Aromatic Hydrocarbons. C9 Rich Aromatic Hydrocarbons are structurally similar to C_9AHM which is predominantly composed of C_9 aromatic hydrocarbon materials such as propylbenzenes, methyl-ethylbenzenes and trimethylbenzenes. On average, C9 Rich Aromatic Hydrocarbons contain 94 percent C_9 aromatic hydrocarbons. Consequently, since aromatic fluids can be considered valid analogues of each other for purposes of predicting toxicity as discussed above, C_9AHM can be considered a valid analog for C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons.

Subchronic oral and inhalation exposure studies indicate Aromatic 100, 150 and 200 Fluids to be relatively non-toxic except at high doses. Reversible effects to the liver, thyroid, stomach, spleen, and urinary bladder were reported mid- and high doses in a subchronic oral toxicity study in rats. A developmental inhalation study in mice indicates severe maternal and developmental toxicity at the high dose (1500 ppm) and reduction in fetal weight gain at the next lowest dose (500 ppm) but no other evidence of developmental effects nor any adverse effects in maternal animals. An oral developmental study in rats indicates maternal effects (decreased body weight gain and food consumption) at the mid-dose (150 mg/kg/day) but no developmental effects at the highest dose tested (450 mg/kg/day). An inhalation reproduction study in rats indicates reduced body weight gain in parents and off-spring at mid and high doses (500 and 1500 ppm) and reduced parental weight gain at 100 ppm in the F_2 generation. Based on neurotoxicity studies, Aromatic 100, 150, and 200 Fluids are not expected to cause any nervous system damage.

Naphthalene was subject to an EPA IRIS assessment in 1998. In that assessment, EPA adopted a chronic reference dose health benchmark based on a subchronic oral toxicity study and a reference concentration for chronic inhalation exposure based on a chronic mouse inhalation study. EPA's IRIS assessment for naphthalene does not include an acute health benchmark because no effect attributable to a single day oral exposure was observed in animal studies. Naphthalene is currently classified by EPA/IRIS as a "possible" (Group C) human carcinogen (no cancer quantification required) and by IARC as "possibly carcinogenic to humans" (Group 2B). It should be noted that the carcinogenicity classification of naphthalene is currently being reviewed as part of EPA's ongoing update of the Integrated Risk Information System (IRIS) program.

Aromatic 100, 150, and 200 Fluids are of low toxicity for endpoints of concern for developmental and reproductive effects, based on the available information. Reproductive and developmental studies show no sensitivity issues of concern. Therefore, the tenfold FQPA safety factor for the protection of infants and children may be reduced to 1 for these compounds.

4.3 Summary of Toxicity Studies

4.3.1 Aromatic 100, 150, and 200 Fluids

Metabolism

Due to their complex, multi-constituent nature, there are no absorption, metabolism, distribution and excretion studies done specifically on these Aromatic Fluids. However, sufficient data on other aromatic solvents – such as alkylbenzenes and alkylnaphthalenes – exist to describe the absorption, distribution, metabolism and excretion of Aromatic 100, 150, and 200 Fluids (Hissink *et al.* 1999; Snyder 1987; *Patty's Toxicology* 2001; European Union 1999). Typically, aromatics are well absorbed, widely distributed between tissues, extensively metabolized and rapidly excreted. The efficiency of dermal absorption varies depending on the molecular weight and structure of the compounds.

Following absorption, aromatic hydrocarbon solvents distribute throughout the body and are extensively metabolized and eliminated. Typically, the solvents will be found at higher levels in the organs of metabolism and excretion, although they can distribute to other tissues as well, particularly those with high lipid content.

The most common metabolic pathway for aromatic hydrocarbon solvents is oxidation followed by conjugation. Cytochrome P450 catalyzes the oxidation of the solvents to alcohol or acidic forms. For compounds with side chains – including the trimethylbenzenes, propylbenzenes, and methyl-ethylbenzenes that are the predominant constituents of Aromatic 100 Fluid – side chain oxidation is the first step in metabolism. Glucuronidation and sulfation are both common Phase II reactions in the metabolism of heavy aromatic hydrocarbon solvents, and these reactions typically occur in the liver. Other conjugation reactions also may occur. This conjugation typically serves to detoxify the heavy aromatic hydrocarbon solvent metabolites, and the conjugates often can be found in the urine.

Aromatic hydrocarbon solvents are rapidly excreted. Both rodents and humans show similar clearance kinetics of hydrocarbons from blood. Typically, they are excreted as various metabolites in the urine, although some parent compound may still be present. Urine is the primary route of excretion for hydrophilic conjugates from both oral and inhalation exposure to aromatic hydrocarbon solvents, although a much smaller fraction of metabolite excretion can also occur through the feces. Some lower molecular weight components of heavy aromatic hydrocarbon solvents – including some of the compounds in Aromatic 100 Fluid – may also be excreted through the lung. In radiotracer experiments, most heavy aromatic hydrocarbon solvents are almost completely eliminated from the body within 48 hours, although small amounts may reside in organs with high lipid content for slightly longer periods of time.

Subchronic Toxicity

In a subchronic oral gavage study, Solvesso® 200 Fluid was administered to Sprague-Dawley rats at concentrations of 300, 600 or 1000 mg/kg/day, 7 days/week for 13 weeks (MRID 46398905, EMBSI 1991). A satellite group received 1000 mg/kg/day for 13 weeks, followed by a 4-week recovery period. Body weights and food consumption were significantly decreased in male rats at 1000 mg/kg/day; this effect was not seen in female rats. Hematologic and serum chemistry changes were observed in both male and female rats at 600 and 1000 mg/kg/day dose levels and correlated with effects seen in the liver and spleen. Kidney and liver weights increased in both sexes and all dose levels but the organ weights for animals in the recovery group were similar to those of control animals, indicating that this was a reversible effect. No treatment related histopathological effects were observed in the kidney. Treatment related microscopic changes were observed in the liver, thyroid, stomach, spleen and urinary bladder of rats. Histopathologic effects included liver hypertrophy that was observed in the females at all dose levels and sporadically in males. The effects had reversed completely in the recovery group animals. Thyroid hyperplasia and hypertrophy of the follicular epithelial cells were observed in male and female rats at all doses. The effects were also observed in the control animals at a similar severity level, but at a lower incidence rate. After the recovery period, the severity and incidence of the effects were comparable in control and test animals. Hemosiderosis was observed in the spleen of males and females at 600 and 1000 mg/kg/day. Hyperplasia of the urinary bladder mucosa was observed in male rats at all doses and in female rats at 600 and 1000 mg/kg/day. The effects in the spleen and urinary bladder were reduced in the recovery group animals. Inflammation and necrosis of the stomach were observed in some treated animals and were attributed to the effects of intubation of a locally irritating substance on the gastrointestinal tract. The effects had reversed completely after the 4-week recovery period. The NOAEL is 300 mg/kg/day based on reversible treatment-related microscopic changes observed in the liver, thyroid, stomach, spleen, and urinary bladder in both male and female rats at 600 and 1000 mg/kg/day.

The subchronic toxicity of 1,3,5-trimethylbenzene (which may be present in high concentrations in some aromatic hydrocarbons) was evaluated in a 90-day oral gavage study in rats (IIT Research Institute 1995). Sprague Dawley rats were dosed at levels of 0, 50, 200 and 600 mg/kg/day. A satellite groups received 600 mg/kg/day and was held for a 28-day recovery period. There were no treatment-related deaths during the study. (Two animals died due to dosing errors.) There was a statistically significant decrease in body weight gain in the high dose males at the end of Week 5; although weight gain in the high dose males was still decreased compared to controls at the end of the treatment period, cumulative body weight gain was not significantly different in treatment versus control animals. In addition, cumulative body weight gain in the recovery animals at the end of the 28-day recovery period was similar to control animals. The only significant changes observed were increased phosphorous levels and alterations in liver and kidney weights in high dose animals. At the end of the 28-day recovery period, these effects were no longer observed, indicating that they are reversible. These effects were considered an adaptive response and therefore not an adverse effect from exposure to the test material. Based on the results of this study, the NOAEL was 600 mg/kg/day, the highest dose tested.

In one study, rats were exposed via inhalation to a 50/50 mixture of Solvesso® 100 Fluid and Shellsol® A at 450, 900, and 1800 mg/m^3 for 6 hours/day, 5 days/week for twelve months (Clark et al. 1989). Transient changes in hematologic and plasma clinical chemical parameters and increased liver and kidney weights were observed at the highest dose only. No corresponding histopathological differences or evidence of exposure-related kidney dysfunction were observed, leading the study researchers to conclude that the observed effects were physiological adaptive responses and not biologically significant. The study NOAEL was greater than 1800 mg/m^3.

<u>Developmental and Reproductive Toxicity</u>

C_9AHM was evaluated in a mouse inhalation developmental toxicity test (McKee *et al.* 1990). Pregnant mice were exposed to 100, 500, or 1500 ppm for 6 hr/day from days 6-15 of gestation. Exposure to 1500 ppm produced severe maternal toxicity - 44% mortality. At 500 ppm there was significantly reduced maternal weight gain and one unexplained death. There was no maternal toxicity at the 100 ppm level. Exposure to 1500 ppm produced fetal effects including mortality, reduced body weight, delayed ossification and an increased incidence of cleft palate. Exposure to 500 ppm resulted in a significant reduction in fetal weight gain, but no other evidence of developmental effects. No developmental toxicity occurred at the lowest dose level (100 ppm). On this basis, the NOAEL for both maternal and developmental effects is 100 ppm. The maternal and developmental LOAELs are 500 ppm based on reduction in maternal weight gain and reduced fetal weight gain respectively.

Solvesso® 200 Fluid was evaluated in a Sprague Dawley rat developmental study (EMBSI 1992). Pregnant dams were dosed by oral gavage with 75, 150 or 450 mg/kg/day during gestational days 6 through 15. At 450 mg/kg/day, maternal body weight gain and food consumption were significantly decreased during the first three days of treatment. Mean body weight change was comparable between treated animals and controls during the overall study period, and there were no statistically significant differences in organ weights and uterine implantation data between treated groups and controls. There were no adverse fetal effects at any dose. There were no differences in mean fetal body weight, nor were there any significant differences in the incidences of fetal variations or malformations in treated groups as compared to controls, either on a per fetus or a per litter basis. Based on the study results, the maternal NOAEL is 150 mg/kg/day. The maternal LOAEL is 450 mg/kg/day based on decreased body weight gain and food consumption. The developmental NOAEL for this study is greater than 450 mg/kg/day, the highest dose tested.

C_9AHM was evaluated in a three-generation reproduction inhalation study in rats at 0, 100, 500, or 1500 ppm (McKee *et al.* 1990). Male fertility was significantly reduced in the F_1 males in the 1500 ppm group. However, as fertility was not affected in the first and third generation, this effect was not considered by the study authors to have been related to exposure. Exposure at the mid- and high-dose levels resulted in reduced parental weight gain in both the F_0 and F_1 generations. For F_2 rats, weights of both males and females were initially below control values in the 100 and 500 ppm group. F_1 and F_2 litters showed significant reductions in mean pup weights at the high dose only; similar effects were seen in the F_3 litters at both mid and high dose. However, when parental exposure was stopped just prior to delivery on gestational day 20, birth weights as well as postnatal weight gain were similar to control values even in the 1500 ppm exposure group. Postnatal weight gain was also similar to control values early in weaning, but if maternal exposure was reinitiated, weight gain was reduced in the high exposure group. When exposure was continued until delivery, pups in the high exposure group exhibited reduced litter size, birth weight and poor survival. There was no increase in developmental variations for offspring at any dose level. Based on the foregoing, the NOAEL and LOAEL for reproductive effects are 500 and 1500 ppm respectively. The LOAEL for parental system toxicity is 500 ppm in the F_0 and F_1 and generations and 100 ppm in the F_2 generation based on reduced parental weight gain. The NOAEL for F_0 and F_1 generations is 100 ppm. The parental NOAEL for the F_2 generation is below the lowest dose tested of 100 ppm. The NOAEL for offspring toxicity is 500 ppm in the F_1 and generations, and 100 ppm in the and F_3 generation. The LOAEL for offspring toxicity is 500 ppm based on significant reductions in mean pup weights at both mid and high doses.

Neurotoxicity

A subchronic neurotoxicity test exposed Sprague Dawley rats to 0, 101, 452 or 1320 ppm C_9AHM 6 hours per day, 5 days per week for 90 days (Douglas *et al.* 1993). Body weights of the high dose group were depressed as compared to controls for much of the exposure period. However, by the end of the post-exposure period, these differences were not statistically significant. No overt signs of toxicity were observed, and histopathological examination showed no evidence of neuropathological or degenerative changes in the central and peripheral nervous system at the highest dose tested. No exposure related effects were seen in any motor activity or neurobehavioral tests, including quantitative motor activity, startle response, quantitative grip strength, hindlimb splay or thermal response. The NOAEL for this study was 1320 ppm.

A neurobehavioral testing program on aliphatic, cycloaliphatic and aromatic hydrocarbons was conducted by the CEFIC Hydrocarbon Solvent Producers Association (Nessel *et al.* 2000; TNO Nutrition and Food Research Institute 2001). The purpose of this program was to develop data on the neurobehavioral effects of hydrocarbon solvent constituents on the central nervous system. Twelve representative constituents of complex hydrocarbon solvents, with carbon chain lengths ranging from C_5- C_{11}, were evaluated. Most representative for purposes of evaluating the toxicity of the Aromatic Fluids was the test on C_{10}-C_{11} Aromatics. Male rats were exposed by inhalation, 8 hours per day for 3 consecutive days to 0, 35, 110 or 365 ppm (0, 0.2, 0.6 and 2.0 g/m^3). Animals were tested for effects on motor activity, functional observation measures, and learned performance of a visual discrimination task. No remarkable clinical signs were observed during the testing period. Some low to moderate gait abnormalities were observed during the 3-day exposure period in rats exposed at the maximum concentration level. In the learned performance test, the high dose rats had increased latencies to make a correct choice and latencies to obtain water reinforcement, as well as increases in the variability of the speed of responding. A small, but statistically significant, decrease in the number of collected reinforcements also was observed in the high dose group. Effects of exposure were most clearly observed after the first eight-hour exposure period. The LOAEL for this test was 365 ppm (2.0 g/m^3), and the NOAEL was 110 ppm (0.6 g/m^3).

These two studies suggest that Aromatic 100, 150, and 200 Fluids can cause slight, transient central nervous system depression, with related minor neurobehavioral effects. However, based on these studies, they are not expected to cause nervous system damage.

Chronic Toxicity/Carcinogenicity

Aromatic 100, 150 and 200 Fluids have not been tested specifically for carcinogenicity. However, registrant submitted data on the structure and metabolism, subchronic health effects, and genotoxicity of these compounds indicate that they are not likely to have carcinogenic properties. Aromatic 100, 150 and 200 Fluids do not belong to a class of chemicals known to react with DNA, nor are they metabolized to materials that are likely to react with DNA. Materials which are oncogenic for mammals appear to cause cancer either by interacting with the genetic material (DNA) (that is, they are genotoxic and, therefore, are probably initiators of the carcinogenic process), or they produce chronic toxic effects which result in increased cell turnover and, therefore, produce effects by epigenetic mechanisms and are probably promoters of the carcinogenic process. The data available for Aromatic 100, 150 and 200 Fluids indicate that these compounds are not genotoxic. Aromatic fluids containing primarily C_9AHM have been tested for mutagenic activity in the following *in vitro* tests: bacterial reverse mutation assay; CHO gene mutation assay; CHO sister chromatid exchange assay; and CHO/HGPRT forward mutation suspension assay (Schreiner *et al* 1989). In addition, C_9AHM was tested in an *in vivo* bone marrow chromosomal aberration test (Schreiner *et al.* 1989). There was no indication of mutagenic activity in any of the assays, providing strong support for the conclusion that Aromatic 100 Fluid is not likely to be mutagenic. Further, in its evaluation of C_9AHM as part of a TSCA Section 4 test rule, EPA concluded that, based on the negative mutagenicity studies and other available data, no further mutagenicity or carcinogenicity testing of these compounds was required. (EPAs "Review of Mutagenicity Testing Results on C_9 Aromatic Hydrocarbon Fraction" April 1, 1992 concluded, "The negative results of these studies do not trigger additional mutagenicity or carcinogenicity testing as specified in the C_9 test rule."). Based on this data, C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are considered unlikely to be carcinogenic.

4.3.2 Naphthalene

Metabolism

The metabolism of naphthalene has been extensively investigated and reported in the literature (Buckpitt and Franklin, 1989; Wells *et al.* 1989; Plopper *et al.* 1992a, b; Xu *et al.* 1992a,b; Wilson *et al.* 1996; Chichester *et al.* 1994; IARC 2002). The initial step in the metabolism of naphthalene in mammalian species is oxidation, catalyzed by cytochrome P450 oxygenases (CYP2F family), to naphthalene1,2-epoxide (also called naphthalene 1,2-oxide); both the 1R,2S and 1S,2R enantiomers may be formed, depending on the P450 isoform. The epoxide may undergo the following transformations: (1) be enzymatically conjugated with glutathione by glutathione S-transferases to form a variety of glutathione conjugates that are excreted in the urine as n-acetylcysteine; (2) be enzymatically hydrated by epoxide hydrolase to form naphthalene-1,2-dihydrodiol, which can be conjugated with sulfate and glucuronic acid, or converted by catechol reductase, forming naphthoquinone via oxidation; (3) spontaneously rearrange to form naphthols (primarily 1-naphthol) and eventually form naphthalene diols and naphthoquinones; or (4) react with nucleophilic cellular constituents (EPA, 1998; Franklin 1987; Klaassen 1996). The first two pathways generally are considered to detoxify naphthalene 1,2-epoxide.

Subchronic

The IRIS health assessment of naphthalene (EPA, 1998)cites a subchronic oral toxicity study in rats as its principal study in determining an reference dose for chronic oral exposure. In the cited subchronic oral toxicity study, naphthalene was administered by gavage to Fischer 344 rats at dose levels of 0, 25, 50, 100, 200, or 400 mg/kg, 5 days/week for 13 weeks (BCL, 1980). Animals were evaluated for food consumption and body weight, clinical signs of toxicity and hematological parameters (hemoglobin, hematocrit, total and differential white blood cell count, red blood cell count, mean cell volume, mean cell hemoglobin concentration), as well as necropsy of all rats in the study, and histopathological examination of selected animals.

At the highest dose level, there were overt signs of toxicity, including death of two animals, and diarrhea, lethargy, hunched posture, and rough coats at intermittent intervals throughout the study. Food consumption was not affected by exposure, but mean decreases in terminal body weight were observed in the 200 and 400 mg/kg/day dose groups. Some differences in hematological parameters also were observed in the high dose group, and some histopathological effects were noted in the kidney and thymus of high (and some mid) dose animals. Decreased body weight was the most sensitive effect and EPA identified this effect as the most appropriate critical effect for the purposes of RfD derivation. The study NOAEL was 100 mg/kg/day.

Developmental

Developmental effects were summarized in the IRIS Toxicological Review of Naphthalene as follows. In developmental toxicity studies, naphthalene was administered by gavage to pregnant animals during gestation, and little evidence was found of naphthalene fetal developmental toxicity. Signs of maternal toxicity (e.g., decreased body weight gain, lethargy) without fetal effects were found in a rat study (NTP, 1991) and a rabbit study (NTP, 1992). Other studies were conducted at dose levels that either produced increased maternal mortalities (mice: Plasterer et al., 1985; rabbits: NTP, 1990) or no maternal or fetal effects (rabbits: Naismith and Matthews, 1985)

Chronic/Cancer

Naphthalene is currently classified by EPA as a "possible" (Group C) human carcinogen (no cancer quantification required). This is based on the inadequate data of carcinogenicity in humans exposed to naphthalene via the oral and inhalation routes, and the limited evidence of carcinogenicity in animals via the inhalation route. Using the 1996 Proposed Guidelines for Carcinogen Risk Assessment, the human carcinogenic potential of naphthalene via the oral or inhalation routes "cannot be determined" at this time based on human and animal data; however, there is suggestive evidence (observations of benign respiratory tumors and one carcinoma in female mice only exposed to naphthalene by inhalation (NTP, 1992a)). Additional support includes increase in respiratory tumors associated with exposure to 1-methylnaphthalene. At the present time the mechanism(s) whereby naphthalene produces benign respiratory tract tumors are not fully understood, but are hypothesized to involve oxygenated reactive metabolites produced via the cytochrome P-450 monooxygenase system. However, based on the many negative results obtained in genotoxicty tests, a genotoxic mechanism appears unlikely. An oral slope factor for naphthalene was not derived by EPA because of a lack of chronic oral naphthalene studies. An inhalation unit risk estimate for naphthalene was not derived by EPA because of the weakness of the evidence (observations of predominant benign respiratory tumors in mice at high dose only) that naphthalene may be carcinogenic in humans. Naphthalene is classified by IARC as "possibly carcinogenic to humans" (Group 2B). It should be noted that the carcinogenicity classification of naphthalene is currently being reviewed as part of EPA's ongoing update of the IRIS program.

4.4 Special Considerations for Infants and Children

C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are of low toxicity for endpoints of concern for developmental and reproductive effects, based on the available information. Therefore an additional tenfold safety factor for the protection of infants and children is determined to be unnecessary.

4.5 Endpoint Selection

4.5.1 C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons

Acute RfD

For acute dietary exposure, an oral NOAEL of 150 was selected from a rat developmental gavage study based on significantly decreased maternal body weight gain and food consumption during the first three days of treatment at the LOAEL of 450 mg/kg/day. An uncertainty factor (UF) of 100x (10x for interspecies and 10x for intraspecies is extrapolation) was applied which results in an RfD of 1.5 mg/kg/day. The study and the end point are considered appropriate for the route and duration.

$$\text{Acute RfD} = \frac{150 \text{ mg/kg/day}}{100 \text{ (UF)}} = 1.5 \text{ mg/kg/day}$$

Chronic RfD

For chronic dietary exposure for all populations, the oral NOAEL of 150 was selected from the rat developmental gavage study based on significantly decreased maternal body weight gain and food consumption during the first three days of treatment at the LOAEL of 450 mg/kg/day. An uncertainty factor (UF) of 100x (10x for interspecies and 10x for intraspecies is extrapolation) was applied which results in an RfD of 1.5 mg/kg/day. The study and the end point are considered as the most appropriate for chronic dietary exposure given that effects in longer term studies were seen only at higher doses.

$$\text{Chronic RfD} = \frac{150 \text{ mg/kg/day}}{100 \text{ (UF)}} = 1.5 \text{ mg/kg/day}$$

Short Term Inhalation

For short-term inhalation, the toxicology endpoint was selected from a 3 day inhalation neurobehavioral testing program in rats on twelve representative constituents of complex hydrocarbon solvents, with carbon chain lengths ranging from C_5- C_{11}. The NOAEL for this study was 110 ppm (156 mg/kg/day) based on low to moderate gait abnormalities observed at the maximum concentration level of 365 ppm. This inhalation study is considered the most appropriate for endpoint selection based on the expected duration of exposure (short-term). The level of concern (LOC) or target margin of exposure (MOE) for inhalation exposures is 100 based on the conventional uncertainty factor of 100X (10x for interspecies and 10x for intraspecies is extrapolation).

Short Term Dermal

For short term dermal exposure, the oral NOAEL of 150 was selected from the rat developmental gavage study based on significantly decreased maternal body weight gain and food consumption during the first three days of treatment at the LOAEL of 450 mg/kg/day. The LOC or MOE) for dermal exposures is 100 based on the conventional uncertainty factor of 100X.

Dermal Absorption

A dermal absorption estimate of 5% was selected based on the dermal absorption of ethyl benzene in hairless mice (Susten et al, 1990). Ethyl benzene is a vaporous compound analogous to the Aromatic Fluids.

Incidental Oral

No dose or endpoint selected for incidental oral because oral post-application exposure is expected to minimal. Only a small fraction of the compounds are expected to remain on the ground or grass because Aromatic Fluids tend to evaporate rapidly.

Table 6. Summary of Toxicological Doses and Endpoints for C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary All Populations	NOAEL= **150** mg/kg/day UF = **100** **Acute RfD** = **1.5** mg/kg/day	FQPA SF = **1X** **aPAD** = acute RfD / FQPA SF = **1.5** mg/kg/day	Developmental Oral- Rat Maternal LOAEL = 450 mg/kg/day based on decreased body weight gain and food consumption
Chronic Dietary All Populations	NOAEL= **150** mg/kg/day UF = **100** **Chronic RfD** = **1.5** mg/kg/day	FQPA SF = **1X** **cPAD** = chronic RfD / FQPA SF = **1.5** mg/kg/day	Developmental Oral- Rat Maternal LOAEL = 450 mg/kg/day based on decreased body weight gain and food consumption
Inhalation - Short-term	NOAEL = 110 ppm (146 mg/kg/day)*	Residential LOC for MOE = 100	3 Day Inhalation Nuerobehavoiral Testing Program - Rat LOAEL = 365 ppm based on low to moderate gait abnormalities
Incidental Oral	Endpoints of concern were not selected for incidental oral exposure scenarios based on physical-chemical property data.		
Dermal - Short-term	NOAEL= **150** mg/kg/day (dermal absorption rate = 5%)	Residential LOC for MOE = 100	Developmental Oral- Rat Maternal LOAEL = 450 mg/kg/day based on decreased body weight gain and food consumption
Cancer Oral, Dermal, Inhalation	Not likely to be carcinogenic in humans		

* MW of C_9AHM = 129

4.5.2 Naphthalene

Acute RfD

EPA's IRIS assessment for naphthalene does not include an acute health benchmark because no effect attributable to a single or few day(s) oral exposure was observed in animal studies.

Chronic RfD

The chronic RfD for naphthalene was selected based on information provided in IRIS. The toxicology endpoint was selected from a subchronic oral gavage study in rats in which the NOAEL was 71 mg/kg/day based on decreased mean terminal body weight in males at the LOAEL of 143 mg/kg/day. A UF of 3000x was considered appropriate for deriving the chronic RfD (10 to extrapolate from rats to humans; 10 to protect sensitive humans; 10 to extrapolate from subchronic to chronic exposure; and 3 for data base deficiencies to arrive at a chronic RfD of 0.02 mg/kg/day.

$$\text{Chronic RfD} = \frac{71 \text{ mg/kg/day}}{3000 \text{ (UF)}} = 0.02 \text{ mg/kg/day}$$

Dermal and Incidental Oral Endpoints

No dose or endpoints were selected for dermal or incidental oral exposure for naphthalene because exposures via these routes are expected to minimal due to high and rapid evaporation rates and predicted low dermal absorption.

5.0 Exposure Assessment

5.1 Dietary Exposure and Risk Assessment

To assess whether C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons meet the standard for reissuance of a tolerance exemption, HED conducted a dietary exposure and risk assessment using the Screening-Level Dietary Exposure Model for Inert Ingredients developed jointly by the Inerts Team and residue chemists in HED. Anticipated residues of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons were compared to modeled anticipated residues for inerts which were derived based on the inert ingredients screening model.

The Tier 1Inert Ingredient Model assessment is based on the following assumptions: actual crop-specific residue data for active ingredients can be utilized as surrogate data for inert ingredient residue levels (including secondary residues in meat, milk, poultry and eggs); inert ingredients are used on all crops and 100% of all crops are "treated" with inert ingredients; no adjustment made for percent of inert in formulation, application rate, or multiple applications of different active ingredient formulations; and only preharvest applications are considered.

The Inert Ingredient Model exposure estimates are based on highest tolerance level residues of high-use active ingredients for all food forms, including meat, milk, poultry, and eggs. A group of 57 of the most "significant" active ingredients were considered. These active ingredients included substances in the insecticide, fungicide, and herbicide class and were selected based on a overall ranking scheme that included the following components. Overall use from 1999 data for active ingredient use (in lbs/yr) – all herbicides at >5 million lbs/yr and all fungicides and insecticides at > 1 million lbs/yr were included. All active ingredients used on crops that are significant contributors to diet were included (i.e., all which had substantial use on crops that make up the "Top 25" childrens diet). Crop-by-crop pesticide use information was evaluated to identify the most frequently used active ingredients. Data from actual residue monitoring studies from active ingredients with the highest frequency of detection were used. Tolerances for the 57 active ingredients were examined for each of the representative crops in the Agency's crop group designations [40 CFR 180.41] and for all crops not included in a crop group. Where there were multiple tolerances for a given crop or commodity, the highest tolerance was chosen as the residue level for the model. Non-representative crops within each crop group were matched to their most-closely related representative crop based on OPP/HED's standard operating procedure 2000.1 USEPA, 2000).

Tier 1 generic inert ingredient acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. For this screening-level assessment, only a Tier 1 analysis was performed.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day. This procedure is performed for each population subgroup. A DEEM™-type analysis was performed utilizing the highest established tolerance level residue for each commodity. In those cases where DEEM listed a commodity for which a published tolerance did not exist, the input value was selected based on representative crops or other "default" values (e.g, use of standard processing factors). A DEEM-FCID™, Version 1.3 analyses were performed for both acute and chronic dietary exposure scenarios and the results for each are given in Table 7.

The results of this Inert Ingredient Screening Model should represent an upper-bound estimate of likely potential dietary exposure to an inert ingredient resulting from preharvest use. For this assessment of C9 Aromatic Hydrocarbons, C10-11Aromatic Hydrocarbons, and C11-12 Aromatic Hydrocarbons, these values were compared to the selected toxicity endpoints using the percent of Population Adjusted Dose (%PAD) approach.

Table 7. Estimated Acute and Chronic Dietary Exposure[1] for a Generic Inert.

Population Subgroup	Estimated Acute Exposure (mg/kg/day)			Est Chronic Exposure (mg/kg/day)
	95th Percentile	99th Percentile	99.9th Percentile	Average
U.S. Population (total)	0.336	0.643	1.164	0.120
All infants (< 1 year)	0.701	1.060	2.056	0.245
Children (1-2 years)	0.939	1.382	2.106	0.422
Children (3-5 years)	0.683	1.010	1.476	0.310
Children (6-12 years)	0.395	0.563	0.827	0.174
Youth (13-19 years)	0.239	0.357	0.815	0.100
Adults (20-49 years)	0.199	0.295	0.468	0.087
Adults (50+ years)	0.191	0.263	0.357	0.086
Females (13-49 years)	0.198	0.287	0.415	0.087

[1] Exposure estimates are based on highest-tolerance-level residues of high-use active ingredients for all food forms, including meat, milk, poultry, and eggs.

The Tier 1screening assessment does not account for evaporative loss which is a particularly important consideration for volatile compounds such as the Aromatic Hydrocarbons. Based on information provided by ExxonMobil, HED conducted a Tier 2/Tier 3 assessment which still retains conservative assumptions regarding application rates, percent crop treated, etc., but which more accurately reflects the evaporative loss of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons.

To assess the impact of evaporative loss on dietary exposures to C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons, ExxonMobil conducted an assessment of the evaporative loss of Aromatic 150 and 200 Fluids using ASTM Method D3539. Following ASTM D 3569 protocol relative evaporation rates (as compared to n-butyl acetate) result in calculated neat evaporation rates of 7.29E-7 g/s/cm^2 and 2.73E-8 g/s/cm^2 for Aromatic 150 and 200 Fluids respectively. As noted by ExxonMobil, these results indicate a significant potential for evaporative loss of Aromatic Hydrocarbons from treated agricultural surfaces (e.g., foliage).

Application of a 98% loss factor to the Tier 1 Inerts Model residue values, as proposed by the registrant based on the ASTM data, results in exposures significantly below OPP's level of concern for acute (at 99.9 % of the aPAD) and chronic exposures as shown in Table 8. Use of a evaporation loss factor as low as 50% would still result in exposures well below the level of concern.

Table 8. Estimated Acute and Chronic Dietary Exposure for a C9, C10-11, and C11-12 Rich Aromatic Hydrocarbons

Population Subgroup	Acute Dietary Exposure			Chronic Dietary Exposure		
	aPAD (mg/kg/day)	Exposure (mg/kg/day)	99.9^{th} ile % aPAD	cPAD (mg/kg/day)	Exposure (mg/kg/day)	Mean % cPAD
U.S. Population (total)	1.5	0.0233	1.6	1.5	0.0016	0.2
All infants (< 1 year)	1.5	0.0411	2.7	1.5	0.0033	0.3
Children (1-2 years)	1.5	0.0421	2.8	1.5	0.0056	0.6
Children (3-5 years)	1.5	0.0295	2.0	1.5	0.0041	0.4
Children (6-12 years)	1.5	0.0165	1.1	1.5	0.0023	0.2
Youth (13-19 years)	1.5	0.0163	1.1	1.5	0.0013	0.1
Adults (20-49 years)	1.5	0.0094	0.6	1.5	0.0012	0.1
Adults (50+ years)	1.5	0.0071	0.5	1.5	0.0011	0.1
Females (13-49 years)	1.5	0.0083	0.6	1.5	0.0012	0.1

The results of this assessment indicate that both acute and chronic dietary risks are well below OPP's level of concern. This assessment should represent an upper-bound estimate of likely potential dietary exposure to C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons as inert ingredients resulting from preharvest use. As stated in the documentation for the Inert Screening Model, in cases where this model would yield dietary risk values below the level of concern, no further refinements are necessary, and the potential dietary exposure and risk are considered adequately characterized.

A chronic dietary exposure assessment was also conducted for naphthalene using the same methodology described above for assessment the Aromatic Fluids. Dietary exposure to naphthalene was assessed using the same assumptions regarding evaporation rates used for the Rich Aromatic Hydrocarbons dietary assessment. An application rate of 10% of the maximum rate for Rich Aromatic Hydrocarbons was assumed. Based on this assessment, the chronic dietary exposure estimate for the highest exposed population subgroup, children 1-2 years of age, is 4% of the cPAD, and not a of risk concern.

5.2 Environmental Fate Characterization Considerations

C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are expected to rapidly volatilize in air. These compounds are expected to volatilize readily from surface layers of soil and from surface water based on fugacity modeling. C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons readily biodegrade in soil. In a ready biodegradability study in activated sludge, the biodegradation half-life of 1 week; 78% degradation was observed by day 28. Considering their volatilization from surface soils and ready biodegradation, C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are not likely to be present in drinking water sources at substantial concentrations as a result of their use as pesticide inert ingredients.

5.3 Residential Exposure and Risk Assessment

Based on the use patterns associated with C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons as inert ingredients, HED assessed the following residential handler exposure scenarios as representative of the most highly exposed residential pesticide handlers.

1) Mixing, loading, and applying liquid spray formulation to lawns and ornamentals by low-pressure handwand; and
2) Mixing, loading, and applying liquid spray formulation to lawns and ornamentals by hose-end sprayer.

Only outdoor residential exposure scenarios were assessed because, based on information provided by the petitioner, Aromatic Fluids are unlikely to be used indoors due to odor characteristics. Only short-term residential exposures are expected based on the anticipated use pattern. Inhalation and dermal exposures were assessed quantitatively. No dose or endpoints were selected for incidental oral exposure because these exposures are expected to minimal due to the expected rapid evaporation of these Aromatic Hydrocarbons. In accordance with HED policy, data from the Pesticide Handlers Exposure Database (PHED) and or Outdoor Residential Exposure Task Force was used handler exposures in the absence of chemical-specific monitoring data (USEPA, 1998, USEPA, 2000). The following assumptions were made for the exposure and risk calculations:

- Average body weight of an adult handler is 70 kg/day.
- Maximum application rate is 2.2 lb ai per acre based on information submitted by the registrant.
- Area treated is 0.5 acres per day
- Residential handlers are expected to have a short-term exposure duration (less than 30

days).
- Baseline inhalation unit exposure - no respiratory protection.
- Baseline dermal unit exposure - long pants, long sleeved shirts, shoes, and socks.

Results of the residential exposure assessment are provided in Table 9. A target MOE of 100 for the inhalation and dermal routes is considered adequate for the handler risk assessment. Estimated inhalation and dermal MOEs for both handler scenarios are greater than the target MOE of 100 and not of concern.

Table 9. Aromatic 100, 150 and 200 - Short Term Inhalation Exposure & MOEs for Residential Handlers Target MOE = 100									
Exposure Scenario	**Dermal Unit Exposure (mg/kg/day)[1]**	**Inhal Unit Exposure (ug/lb ai)[1]**	**Use[2]**	**Max App Rate[3] (lb ai/acre)**	**Daily Area Treated[4]**	**Dermal Dose (m/k/d)[5]**	**Inhal Dose (m/k/d)[6]**	**Dermal MOE[7]**	**Inhal MOE[8]**
Mixing/Loading/Applying Liquids									
Low Pressure Handwand	100	30	turf/ ornamental	2.2	0.5Acre /day	0.0236	0.0005	6400	300000
Hose-end Sprayer	17	11	turf/ ornamental	2.2	0.5Acre /day	0.0086	0.0002	17000	900000

[1]Baseline inhalation unit exposures represent no respirator. Values are reported in the PHED Surrogate Exposure Guide dated August 1998 or are from data submitted by the Outdoor Residential Exposure Task Force dated May 2000.
Baseline dermal unit exposures represent long pants, long sleeved shirts, shoes, and socks. Values are reported in the PHED Surrogate Exposure Guide dated August 1998 or are from data submitted by the Outdoor Residential Exposure Task Force dated May 2000.
[2] Use patterns are from information provided by the registrant and product labels
[3]Application rates are based on maximum values submitted by the registrant and verified by an HED cursory label review. In most scenarios, a range of maximum application rates is used to represent the range of rates for different crops/sites/uses. Application rates upon which the analysis is based are presented as lb ai/A.
[4]Amount treated is based on the area or gallons that can be reasonably applied in a single day for each exposure scenario of concern based on the application method and formulation/packaging type. (Standard EPA/OPP/HED values).
[5]Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * Dermal absorption (2%) * Application rate (lb ai/acre or lb ai/gallon) * Daily area treated (acres or gallons)] / Body weight (70 kg).
[6]Inhalation dose (mg/kg/day) = [unit exposure (ug/lb ai) * 0.001 mg/ g unit conversion * Inhalation absorption (100%) * Application rate (lb ai/acre or lb ai/gallon) * Daily area treated (acres or gallons)] / Body weight (70 kg).
[7]Dermal MOE = short-term endpoint for dermal - dermal LOAEL (mg/kg/day) / Daily Dermal Dose.
[8]Inhalation MOE = short-term endpoint for inhalation - oral NOAEL (156 mg/kg/day) / Daily Inhalation Dose.

5.4 Aggregate Exposures

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses). Only dietary, dermal and inhalation routes of exposure have been assessed for this analysis for reasons explained above. Inhalation and oral exposures cannot be aggregated for this assessment because the toxicity endpoints selected for the chronic dietary route of exposure and those selected for the inhalation route are not based on common effects. Inhalation and dermal exposures cannot be aggregated for the same reason. Dietary and dermal exposures can be aggregated because the toxicity endpoints selected for these exposure routes are based on common effects. Short term aggregate risks from combined dietary and dermal exposure do not present risks of concern. The aggregate MOE for dietary and dermal exposure is 15000, which significantly exceeds the target MOE of 100. OPP did not conduct an aggregate assessment of risk from the Aromatic Fluids because co-occurrence of these compounds is not expected.

6.0 Cumulative Exposure

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons and any other substances, and these materials do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/

7.0 Ecotoxicity and Ecological Risk Characterization

There is limited measured toxicity information to characterize the effects of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons on aquatic and terrestrial organisms. Data available on Aromatic 100 Fluid show that toxicity values range from non-toxic to slightly toxic to aquatic and terrestrial organisms. C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons are compositionally comparable products as discussed above. Based on a 96 hour fish acute static toxicity test on rainbow trout (*oncorhynchus mykiss*), Aromatic Fluids are classified as slightly toxic, i.e., the lowest 96-hour LC_{50} reported 18.0 mg/L based on nominal values. A 48 hour static daphnid acute toxicity test in the water flea (*daphnia magna*) indicated a classification of slightly toxic based on a 48 hour EL_{50} of 21.3 mg/L (95% Cl 17.2 to 28.9 mg/L). Aromatic Fluids are classified as practically non-toxic to birds based on an acute oral gavage study in Northern Bobwhite Quail, i.e., the acute oral LD_{50} in birds is > 2250 mg/kg. As previously discussed, these chemicals will volatilize readily when released. In addition to volatilization, they will biodegrade readily in soil, which means that run-off into surface water from pesticidal uses is likely to be low. Therefore, based on potential for exposures and available toxicity information, ecological concerns for are not likely to occur from the use of C9 Rich Aromatic Hydrocarbons, C10-11 Rich Aromatic Hydrocarbons, and C11-12 Rich Aromatic Hydrocarbons as pesticide inert ingredients unless application rates exceed 15 lbs./acre annually.

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